with the results of the spectral analysis obtained with said spectral analysis means, said spectral analysis is an infrared spectral analysis and the target drug is at least one selected from the group consisting of an anti-cancer agent, an antibiotic and an anti-viral agent.

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REMARKS

Claims 1-16 were pending in this application and were all rejected by the Office. With entry of this response, claims 1, 3-9, 12, and 16 have been amended, claim 2 has been cancelled, and claims 17-55 have been added. Support for these new claims and amendments is found throughout the originally filed specification and claims.

Objections to the Specification

The Office objects to the specification because the brief description for Figs. 2-7, 9-14, 16-19, and 25-27 do not reference the (A) and (B) portions of each drawing. Office Action, page 2. Applicants have amended the specification accordingly and respectfully request that the Office withdraw this objection.

Indefiniteness Rejections

The Office rejects claims 1-16 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office Action, page 2. Specifically, the Office objects to the use of "and/or" in claims 1-8. Applicants have amended the claims to remove this term.

The Office also contends that "the absorption or emission spectrum" in claims 1, 8, 9, and 16 is indefinite because it lacks proper antecedent basis. Applicants have

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amended the claims to provide proper antecedent basis for the elements in the claims. In view of these amendments, Applicants respectfully request that the Office withdraw the indefiniteness rejections.

Novelty Rejections

The Office rejected claims 1-3 and 8, under 35 U.S.C. 102(b), as allegedly being anticipated by Cohenford *et al.* (WO 97/18566), Oong *et al.* (U.S. Patent No. 5,168,162), or Wong *et al.* (U.S. Patent No. 5,038,039). The Office also rejected claims 1-3 and 7-8, under 35 U.S.C. 102(b), as allegedly being anticipated by Zakim *et al.* (U.S. Patent No. 5,733,739). Applicants respectfully traverse these rejections.

For a prior art reference to anticipate, all of the elements of the claims must be shown in a single reference. M.P.E.P. § 2131. The single reference must describe and enable the claimed invention, including all claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the field of the invention. *Crown Operations International, Ltd. v. Solutia Inc.,* 289 F.3d 1367, 1375 (Fed. Cir. 2002).

Applicants contend that none of the prior art documents cited by the Office disclose every element of the presently amended claims. The present claims are directed to methods that diagnose disease or identify compounds based on "the appearance of spectra corresponding to at least two wave numbers." While Cohenford, Oong, Wong, and Zakim describe spectral data for certain biological specimens, they do not identify the specimens based only on two wave numbers. Rather, they merely

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recognize that there are detectable differences in the absorption spectrum from one sample to the next. Applicants invention is based on the use of two specific wave numbers that characterize a given disease or compound.

Thus, Applicants contend that none of the prior art cited by the Office discloses every element of the present claims. Accordingly, Applicants respectfully request that the Office withdraw all of the rejections under 35 U.S.C. § 102.

Obviousness Rejections

The Office rejected claims 1-12 and 16, under 35 U.S.C. 103(a), as allegedly being obvious over JP 285286 [sic], in view of Cohenford *et al.*, Oong *et al.*, or Wong *et al.* ("secondary references") The Office also rejected claims 9-11 and 13-16, under 35 U.S.C. 103(a), as allegedly being obvious over JP 286740, in view of Cohenford *et al.*, Oong *et al.*, or Wong *et al.* Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. In addition, the proposed combination must teach or suggest all of the elements of the claims. *Id.* The Office has failed to satisfy either of these requirements.

Applicants have informed the undersigned that both JP 285286 and JP 286740 describe methods for judging a transformed state of bioactivity in a substance. However, as noted by the Office, the methods in these publications use only a single peak of a specific spectrum to determine the transformed state of bioactivity. They do

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not teach or suggest the use of two or more wave numbers. This is a notable deficiency, because by using two or more peaks for the judgment, a more reliable measurement is achieved. Such an improvement cannot be taught or suggested in the cited prior art documents, which disclose the use of only a single peak.

Cohenford, Oong, and Wong do not account for these deficiencies in JP 285286 and JP 286740. As noted above, these secondary references do not teach or suggest the use of two specific wave numbers to characterize a given disease or compound, as claimed by Applicants. Rather, the references merely highlight that differences exist in the spectral qualities of various biological samples. Consequently, the combination of these secondary references with either JP 285286 or JP 286740 fails to teach all of the elements of the claims.

Applicants also contend that there is no motivation to make the proposed combination of teachings in the first place. The Federal Circuit does not take the requirement for motivation lightly, stating that "the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of ... motivation . . . The showing must be clear and particular." *[emphasis added]* *See In re Dembiczak,* 175 F.3d 994, 999 (Fed. Cir. 1999) (abrogated on other grounds).

In more recent cases, the Federal Circuit has held that determinations of *prima facie* obviousness must be supported by a finding of "substantial evidence". *See In re Zurko*, 258 F.3d 1379, 1386 (Fed. Cir. 2001). Specifically, unless "substantial evidence" found in the record supports the factual determinations central to the issue of

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patentability, the rejection is improper and should be withdrawn. *See Zurko*, 258 F.3d at 1386.

On January 18, 2002, the Federal Circuit again reaffirmed the Office's high burden to establish a *prima facie* case of obviousness. Specifically, the Federal Circuit held that "[t]he factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Sang-Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (internal quotations and citations omitted). Further, consistent with *Zurko,* the Federal Circuit held that "[t]he examiner's conclusory statements ... do not adequately address the issue of a motivation to combine. This factual question is material to patentability, and could not be resolved on subjective belief and unknown authority." *Id.* at 9.

In the present case, the Office has pointed to no motivation that would lead one of skill in the art to make the proposed combinations of teachings. Rather, the Office provides a conclusory statement that:

> "it would have been obvious to one of ordinary skill in the art at the time of the instant invention to compare the spectra taught by JP '286 [and JP '740] between normal and malignant cells at more than one frequency or wave number since any one of Cohenford, Oong, and Wong disclose that the infrared absorption spectra between normal cells and diseased cells differs from one another at multiple frequencies or wave numbers..."

Office Action, page 7; *See also*, page 6. Far from identifying the requisite motivation to modify the teachings of the prior art, this conclusory statement merely presumes what it is required to prove, and is not based on a clear and particular teaching in the art or objective evidence of record. Such conclusory language has been repeatedly rejected

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by the Federal Circuit because it does not provide the "substantial evidence" necessary to establish motivation. *See, e.g., In re Sang-Su Lee, infra.*

Apparently, the Office is simply assuming that the proposed combination should be made because it is feasible to do so. But the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See* M.P.E.P. § 2143.01 ("Fact that the claimed invention is *within the capabilities of one of ordinary skill in the art* is not sufficient by itself to establish a *prima facie* case of obviousness"). Applicants contend that the Office has provided no evidence to suggest the desirability of combining the cited prior art in the proposed manner. Thus, there is no motivation to combine the references.

Lacking evidence of the requisite motivation, Applicants contend that the Office has failed to establish a *prima facie* case of obviousness. Accordingly, Applicants respectfully request that the Office withdraw the obviousness rejections.

SUMMARY

In view of the above amendments and remarks, Applicants submit that this application is in condition for allowance. An early and favorable action is earnestly solicited.

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Please grant any extensions of time required to enter this reply and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: _____

M. Todd Rands
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Dated: May 1, 2003

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APPENDIX

IN THE SPECIFICATION

Please replace the paragraphs on page 6, lines 16-34, with the following:

--[Fig. 2 shows] Figs. 2A and 2B show graphs illustrating the results of performing spectral analysis using cultured cells derived from ascitic liver cancer as a sample.

[Fig. 3 shows] Figs. 3A and 3B show graphs illustrating the results of performing spectral analysis using cultured cells derived from mice breast cancer as a sample.

[Fig. 4 shows] Figs. 4A and 4B show graphs illustrating the results of performing spectral analysis using cultured cells derived from mouse malignant melanoma as a sample.

[Fig. 5 shows] Figs. 5A and 5B show graphs illustrating the results of performing spectral analysis using cultured cells derived from human stomach cancer as a sample.

[Fig. 6 shows] Figs. 6A and 6B show graphs illustrating the results of performing spectral analysis using cultured cells derived from human glioblastoma as a sample.--

Please replace the paragraph on page 7, lines 1-3, with the following:

--[Fig. 7 shows] Figs. 7A and 7B show graphs illustrating the results of performing spectral analysis using cancer cells extracted from a breast cancer patient as a sample.--

Please replace the paragraphs on page 7, lines 9-30, with the following:

--[Fig. 9 shows] Figs. 9A, 9B, and 9C show graphs illustrating changes in energy states caused by destruction of the cell membrane of cancer cells.

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[Fig. 10 shows] Figs. 10A, 10B, and 10C show graphs illustrating changes in energy states caused by heating cancer cells.

[Fig. 11 shows] Figs. 11A and 11B show graphs illustrating the results of performing spectral analysis using normal rat brain (white matter) cells as a sample.

[Fig. 12 shows] Figs. 12A and 12B show graphs illustrating the results of performing spectral analysis using normal rat liver cells as a sample.

[Fig. 13 shows] Figs. 13A and 13B show graphs illustrating the results of performing spectral analysis using normal mouse mammary gland cells as a sample.

[Fig. 14 shows] Figs. 14A and 14B show graphs illustrating the results of performing spectral analysis using normal human bone marrow cells as a sample.--

Please replace the paragraph on page 7, line 35 through page 8, line 1, with the following:

--[Fig. 16 shows] Figs. 16A and 16B show graphs illustrating the results of performing spectral analysis using cisplatin as a sample.--

Please replace the paragraphs on page 8, lines 3-12, with the following:

--[Fig. 17 shows] Figs. 17A and 17B show graphs illustrating the results of performing spectral analysis using carboplatin as a sample.

[Fig. 18 shows] Figs. 18A and 18B show graphs illustrating the results of performing spectral analysis using doxorubicin hydrochloride (Adriacin) as a sample.

[Fig. 19 shows] Figs. 19A and 19B show graphs illustrating the results of performing spectral analysis using nimustine hydrochloride (ACNU) as a sample.--

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Please replace the paragraph on page 8, line 34 through page 9, line 1, with the following:

--[Fig. 25 shows] Figs. 25A and 25B show graphs illustrating the results of spectral analysis in the case of using Escherichia coli as a sample.--

Please replace the paragraphs on page 8, lines 3-9, with the following:

--[Fig. 26 shows] Figs. 26A and 26B show graphs illustrating the results of spectral analysis in the case of using aztreonam (Azactam) as a sample.

[Fig. 27 shows] Figs. 27A and 27B show graphs illustrating the results of spectral analysis in the case of using transplatin as a sample.--

IN THE CLAIMS

Please amend the claims as follows:

1. (Amended) A method for determining at least one of disease type and [/or] condition [determination method comprising:] which comprises analyzing [the] an absorption or emission spectrum in a specific region for cells obtained from a specimen, and determining at least one of the disease type and [/or] condition by using as indices the appearance of spectra corresponding to at least two wave numbers obtained by measuring an absorption or emission spectrum of cancer cells, bacteria or virus, which cells, bacteria or virus cause specific disease within said specific region in accordance with the results of said spectral analysis, and said specific region includes the infrared region.

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3. (Amended) The [disease type and /or condition determination] method according to claim 1 [or 2] that determines whether or not said specimen is cancer.

4. (Amended) The [disease type and /or condition determination] method according to claim 3, wherein one of the wave numbers of the spectra used as said indices is 1261 cm^{-1}.

5. (Amended) The [disease type and /or condition determination] method according to claim 1 [or 2] that determines whether or not said cells have specific bacteria.

6. (Amended) The [disease type and /or condition determination] method according to claim 5, wherein said specific bacteria are drug resistance bacteria.

7. (Amended) The [disease type and /or condition determination] method according to claim 1 [or 2] that determines whether or not said cells are infected by a specific virus.

8. (Amended) [A] An apparatus for diagnosing at least one of disease type and [/or] condition [diagnostic apparatus comprising:] which comprises

spectral analysis means that analyzes [the] an absorption or emission spectrum in a specific region for cells obtained from a specimen, and

diagnostic means that diagnoses at least one of disease type and [/or] condition using as indices the appearance of spectra corresponding to at least two wave numbers obtained by measuring an absorption or emission spectrum of cancer cells, bacteria or virus, which cells, bacteria or virus cause specific disease within said specific region in accordance with the results of the spectral analysis obtained with said spectral analysis means, and said specific region includes the infrared region.

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9. (Amended) A drug screening method comprising: analyzing [the] an absorption or emission spectrum in a specific region for a target drug, and screening said target drug by using as indices the appearance of spectra corresponding to at least two wave numbers obtained by measuring an absorption or emission spectrum of cancer cells, bacteria or virus, which cells, bacteria or virus cause specific disease within said specific region in accordance with the results of said spectral analysis.

12. (Amended) The drug screening method according to claim 11, wherein [one of] the wave number[s] of the spectra used as said indices is at least one of 1261 cm^{-1} [or] and 1163 cm^{-1}.

16. (Amended) A drug screening apparatus comprising:

spectral analysis means that analyzes the absorption or emission spectrum in a specific region for a target drug, and

screening means that screens said target drug using as indices the appearance of spectra corresponding to at least two wave numbers obtained by measuring an absorption or emission spectrum of cancer cells, bacteria or virus, which cells, bacteria or virus cause specific disease within said specific region in accordance with the results of the spectral analysis obtained with said spectral analysis means.

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